

## **REMARKS**

Applicants respectfully request the Examiner to reconsider the present application in view of the foregoing amendments to the specification and claims and the following remarks.

### **Status of the Claims**

Claims 1-8 are pending in the present application. Claims 6-8 are currently withdrawn from consideration. Claim 1 has been amended to remove unnecessary brackets. No new matter has been added by way of the above amendment. Based upon the above considerations, entry of the present amendment is respectfully requested.

In view of the following remarks, Applicants respectfully request that the Examiner withdraw all rejections and allow the currently pending claims.

### **Specification**

The Examiner notes that the first paragraph of the specification does not contain continuing data to which the instant specification claims benefit from. Applicants have amended the present specification in order to overcome this issue.

### **Objections**

The Examiner has objected to claim 1 for including parentheses, which render the claim ambiguous. Applicants have removed the parentheses. Accordingly, Applicants respectfully request that the objection be removed.

### **Issues under 35 U.S.C. § 103(a)**

The Examiner has rejected claims 1-5 under 35 U.S.C. § 103(a) as being unpatentable over Suzuki et al. '730 (US 7,244,730) in view of FDA drug Application No. NDA #019437. Applicants respectfully traverse, and reconsideration and withdrawal of this rejection are respectfully requested.

Legal Standard for Determining Prima Facie Obviousness

MPEP 2143 sets forth the guidelines in determining obviousness. First, the Examiner has to take into account the factual inquiries set forth in *Graham v. John Deere*, 383 U.S. 1, 17, 148 USPQ 459, 467 (1966), which has provided the controlling framework for an obviousness analysis. The four *Graham* factors are:

- (a) determining the scope and content of the prior art;
- (b) ascertaining the differences between the prior art and the claims in issue;
- (c) resolving the level of ordinary skill in the pertinent art; and
- (d) evaluating any evidence of secondary considerations.

*Graham v. John Deere*, 383 U.S. 1, 17, 148 USPQ 459, 467 (1966). Second, the Examiner has to provide some rationale for determining obviousness. MPEP 2143 sets forth some rationales that were established in the recent decision of *KSR International Co. v Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

As the MPEP directs, all claim limitations must be considered in view of the cited prior art in order to establish a *prima facie* case of obviousness. See MPEP 2143.03.

Distinctions over the Cited Art

Applicants respectfully disagree with the Examiner's findings. The present specification describes a problem whereby the decomposition product of the benzamidine derivative represented by Formula (I) is sometimes generated due to coexistence with a formulation additive under humidification/heating conditions in a solid state and due to a high pH state in a liquid state (see page 2, lines 1 to 10 of the present specification and Fig. 1).

Suzuki et al. '730 disclose some benzamidine compounds represented by Formula (I). The FDA Drug Application merely discloses a pharmaceutical composition which comprises amino acids and electrolytes, such as sodium and potassium chloride, in injectable drug formulations.

Applicants respectfully submit that Suzuki et al. '730 and the FDA Drug Application do not recognize or address the specific problem for the benzamidine derivative represented by Formula (I) described above. Because the above problem is not identified by Suzuki et al. '730 and the FDA Drug Application, no solution to the problem is taught by the disclosures of Suzuki et al. '730 and the FDA Drug Application. That is, it is not obvious, based on Suzuki et al. '730 and the FDA Drug Application, that further stabilization of the benzamidine derivative represented by Formula (I) is necessary.

The present invention is based on the surprising discovery that by adding at least one type of electrolyte selected from the group consisting of halide salts of alkaline metal or alkaline earth metal and alkaline metal salts or alkaline earth metal salts of perchloric acid to the benzamidine derivative represented by Formula (I), the benzamidine derivative can be stabilized. The remarkable technical effects and advantages that can be obtained from the present invention, including stability under humid conditions and lowered manufacturing costs, cannot be expected nor are they suggested, taught, or rendered obvious by the Suzuki et al. '730 and the FDA Drug Application references (see page 6, lines 5-12 of the present specification).

Relevant to this § 103(a) rejection, *Graham v. John Deere*, 383 U.S. 1, 17, 148 USPQ 459, 467 (1966) has provided the controlling framework for an obviousness analysis, wherein a proper analysis under § 103(a) requires consideration of the four *Graham* factors. One such factor includes the evaluation of any evidence of secondary considerations (e.g., commercial success; unexpected results). 383 U.S. at 17, 148 USPQ at 467. In this regard, Applicants respectfully submit that the present invention has achieved unexpected results, whereby such results rebut any asserted *prima facie* case of obviousness. See *In re Corkill*, 711 F.2d 1496, 226 USPQ 1005 (Fed. Cir. 1985). Also, the comparative showing need not compare the claimed invention with all of the cited prior art, but only with the closest prior art. See MPEP 716.02(b) and 716.02(e).

In this regard, Applicants note MPEP 2144.08(5)(B), which states that rebuttal evidence and arguments can be presented in the specification, *In re Soni*, 54 F.3d 746, 750, 34 USPQ2d 1684, 1687 (Fed. Cir. 1995).

Experimental data in the specification, as shown in Tables 2-3, show that the increase in the amount of impurity was inhibited in the present invention, as compared to the composition in which NaCl, an electrolyte, was not added. Similarly, Tables 4-5 show that the amount of decomposition product is less in the present invention, as compared to the composition in which no electrolyte was added.

As the Examiner admits, Suzuki et al. '730 do not specifically teach electrolytes. Thus, this reference is very similar to the comparative examples of the present specification. As such, Suzuki et al. '730 cannot claim the unexpected results of the present invention.

Thus, due to the unexpected results as achieved by the present invention, the rejection has been overcome. Reconsideration and withdrawal of this rejection are respectfully requested.

#### **Obviousness-Type Double Patenting**

Claims 1-5 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 13 and 14 of U.S. Patent No. 7,244,730 (Suzuki et al. '730).

Applicants respectfully submit that the double patenting rejection has been overcome for the reasons given above regarding Suzuki et al. '730. Thus, withdrawal of the outstanding rejection is respectfully requested.

The application is now believed to be in condition for allowance, and an early indication of same is earnestly solicited.

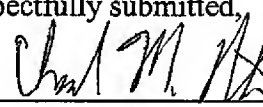
**CONCLUSION**

In view of the above amendment, Applicants believe the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Chad M. Rink, Reg. No. 58,258 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

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